Dysregulation of cardiogenesis, cardiac conduction, and cell cycle in mice lacking miRNA-1-2.

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Authors: Yong Zhao, Joshua F Ransom, Ankang Li, Vasanth Vedantham, Morgan von Drehle, Alecia N Muth, Takatoshi Tsuchihashi, Michael T McManus, Robert J Schwartz, Deepak Srivastava

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Public Summary:

Scientific Abstract:
MicroRNAs (miRNAs) are genomically encoded small RNAs used by organisms to regulate the expression of proteins generated from messenger RNA transcripts. The in vivo requirement of specific miRNAs in mammals through targeted deletion remains unknown, and reliable prediction of mRNA targets is still problematic. Here, we show that miRNA biogenesis in the mouse heart is essential for cardiogenesis. Furthermore, targeted deletion of the muscle-specific miRNA, miR-1-2, revealed numerous functions in the heart, including regulation of cardiac morphogenesis, electrical conduction, and cell-cycle control. Analyses of miR-1 complementary sequences in mRNAs upregulated upon miR-1-2 deletion revealed an enrichment of miR-1 "seed matches" and a strong tendency for potential miR-1 binding sites to be located in physically accessible regions. These findings indicate that subtle alteration of miRNA dosage can have profound consequences in mammals and demonstrate the utility of mammalian loss-of-function models in revealing physiologic miRNA targets.